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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,218	07/24/2006	Marie-Noelle Bizot	4-32908A	4236

67283 7590 12/23/2008

MONTGOMERY, MCCRACKEN, WALKER & RHOADS, LLP
123 SOUTH BROAD STREET
AVENUE OF THE ARTS
PHILADELPHIA, PA 19109

EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
12/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,218	BIZOT ET AL.	
	Examiner	Art Unit	
	Nabila G. Ebrahim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2008*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7-9,13 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7-9,13 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/17/2008 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 5, 7-9, 13, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims1 and 15 recite apple juice and a mixture. The mixture means more than one ingredient while the claims do not recite any mixture but only recite tegaserod or its salt. It is not clear if the recitations omit extra ingredients or there is no mixture with the apple juice. correction or clarification is respectfully required.

The claims are further rejected because claim 1 recites "the suspension provides a partitioning of the effective amount of tegaserod or pharmaceutically acceptable salt thereof". The said partitioning of the effective amount of tegaserod does not clarify if this effective amount is per day or per dose. It is not clear what does the language of the claim as amended include or exclude.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 1, 5, 7-9, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE BRUIJN et al. WO0010526 (De Bruijn) in view of Patel et al. US 20030180352 (Patel) and further in view of the combination of [Achong et al. US 20040162273 (Achong), Belcheff US 20010031283 (Belcheff), Naicker et al US 7060672 (Naicker) and Allen et al. Stability of ramipril in water, apple juice, and applesauce. Am J Health Syst Pharm. 1995 Nov 1;52(21):2433-6, abstract (Allen)].

De Bruijn teaches a pharmaceutical composition, in particular to a composition for administering active agents which are poorly soluble in aqueous media, and/or which are acid sensitive (abstract). The composition comprises tegaserod (pages 5, and 7) or its salt (page 5) and is prepared to have dissolution in water of about 30%-90% in 5 minutes (page 7). The composition could be in the form of tablets among other preparations (page 13). The compositions of the invention were packed in conventional manner to keep out humidity, e.g., in a blister pack, optionally with a desiccant (page 17). Regarding claims 8 and 9 that recite amount of tegaserod in the dosage form of 6 mg or 2 mg. De Bruijn teaches that a tablet may have different amounts according to the condition it is used, for example for irritable bowel syndrome (IBS), 1 mg to 12 mg of active agent is used in the tablet (page 9).

Claims 5-9 recite “a crushed tablet” which reads on a chewable tablet, powder, granulate, bead etc. comprising the tegaserod. From these preparation De Bruijin discloses granulates and compressed tablets (page 19).

New amendments to claim 1

De Bruijn does not teach a crushed tablet or beverage.

Patel teaches solid carriers for improved delivery of active ingredients in pharmaceutical compositions. The composition is meant to mask the taste of unpalatable pharmaceutical active ingredients [0028]. Patel suggests agents of the unpalatable drugs among which is tegaserod [0058] and the dosage form can be a powder or a multiparticulate, such as a granule, a pellet, a bead, a spherule, a beadlet, a microcapsule, a millisphere, a nanocapsule, a nanosphere, a micro sphere, a platelet, a minitablet, a tablet or a capsule [0229]. The composition of the invention can be administered as a chewable tablet, a quick or fast dissolving tablet, an effervescent tablet, a buccal or sublingual solid, a granule, a film, a sprinkle, a pellet, a bead, a pill, a powder, a triturate, a platelet, a strip or a sachet. Compositions can also be administered as" dry syrup", where the finished dosage form is placed directly on the tongue and swallowed or followed with a drink or beverage ([0272], see also claims 24 and 47). The use of water as a beverage is conventional type of a beverage that is usually known and used by the public.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine Patel to De Bruijn because Patel teaches a way for masking the unpleasant taste for the drugs disclosed.

Neither of the references disclosed apple juice as a beverage with the tegaserod.

The combination of Achong, Belcheff, Naicker and Allen are relied upon as follows:

Achong teaches powder pharmaceutical composition. The reference discloses that powder pharmaceutical compositions can also be formulated to contain aesthetically pleasing flavor and sweetener ingredients [0008]. When the powder pharmaceutical compositions can be dissolved in a liquid, such as cold water, ice tea, orange juice, grape juice, and apple juice [0028].

Belcheff teaches a natural extract comprising: providing a quantity of pursiane provided in apple juice which is used as preservative (see claims 1 and 6).

Naicker teaches a pharmaceutical composition comprising cyclosporine analogue dissolved in an aqueous media such as a fruit juice specifically apple juice (see claims 1 and 19) wherein the formulations form stable microemulsion preconcentrates and may provide superior drug bioavailability and/or may reduce one or more adverse effects associated with the administration of cyclosporine (abstract)

Allen researched the stability of ramipril in water, apple juice and applesauce and found that ramipril from 1.25-, 2.5-, and 5-mg capsules mixed in water, and in apple juice was stable for 24 hours at 23 degrees C and for 48 hours at 3 degrees C.

In view of the above explained disclosures, it clear that the art knew the benefits of apple juice as a preservative, a taste masking agent, a bioavailability providing agent, an agent to reduce adverse effects, and a stabilizing agent. Note that the active agents disclosed in the prior arts relied upon are totally different in structure and effect which would motivate a person of ordinary skill in the art to choose from a finite number of predictable option of using apple juice to facilitate swallowing a tablet of tegaserod with a reasonable expectation of success of producing a tegaserod in apple juice formulation. I would also be obvious to a person of ordinary skill to partition the dose of tegaserod because Allen showed that a drug can be stabilized in apple juice for 24 hours and Belcheff teaches that apple juice has a preservative effect.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the tablet disclosed by De Bruijn or Patel's tablet, powder, granulate or crushed tablets to apple juice as disclosed by Achong, Belcheff, Naicker and/or allen because these references disclose that apple juice has an aesthetically pleasing flavor, a preservative property, a taste masking effect, a bioavailability providing property, properties for reducing adverse effects, and a stabilizing agent. The expected result would be a composition

comprising tegaserod or a pharmaceutically acceptable salt swallowed by the use of a beverage or added to a beverage such as apple juice.

The document provided by Applicant as evidence (Exhibit A) was carefully reviewed, however, although it shows that tegaserod can be administered in crushed tablet form in various media and that apple juice appears to be the best of all juices and foods used. It is noted that the instant office action relies upon Achong, Belcheff, Naicker and Allen, wherein the references demonstrate clearly that apple juice is superior to other juices because of the multiple benefits recited **in the claims of the references**. Further, the document concludes that apple juice may be the preferred vehicle because it effectively masks the taste of tegaserod (conclusion). Thus the document provided demonstrates that such apple juice is conventional for a person of ordinary skill in the art to try.

Response to Arguments

1. Applicant's arguments filed 3/28/2008 have been fully considered but they are not persuasive. Applicant argues that:

- neither DeBruijn nor Patel teach, suggest, or provide motivation to use a crushed tablet of tegaserod, or apple juice as a beverage -as recited in Applicant's claims - to form a homogenous oral suspension capable of providing partitioned dosage of tegaserod. Neither DeBruijn nor Patel teach the use of crushed tablets of tegaserod containing a known and fixed amount of active ingredient as a component of a homogenous suspension, wherein the dosage of the active ingredient is capable of being partitioned, as expressly recited by Applicant's claims. Applicant's homogenous oral suspension is an alternative method of tegaserod administration which is especially suitable for partitioning a dosage of tegaserod and for a patient's use at home.

To respond: It is respectfully noted that most of drug formulations are used by patients at home. Being at home while partitioning a tablet and swallowing it or dissolving it in a drink is not inventive or novel. Applicant is arguing an alternative method of administration of tegaserod which is especially suitable for a patient's use at home. However, instant claims are not directed to a method of administering the drug. The claims are directed towards an oral suspension comprising a beverage consisting of apple juice and a mixture consisting of an effective amount of tegaserod or acceptable salt in the form of at least one of a powder, a .granulate, a .grind, and a pulver of particles. DeBruijn's teaches that tegaserod could be prepared in the form of a suspension (page 13), and that the composition is granulated and sieved (see example 1), Patel teaches a crushed tablet of a drug such as tegaserod is suspended in a beverage. Achong and new references (Belcheff, Naicker, and Allen) teach that powder pharmaceutical compositions can be dissolved in a liquid such as apple juice for many advantages such as preservation, stabilization, bioavailability, reducing side effects and taste masking.

- Applicant respectfully asserts that Achong fails to cure the defects of the DeBruijn and Patel combination. There is no teaching, suggestion, or motivation provided by Achong to use the superior dissolution properties of crushed tablets of tegaserod in apple juice, as recited by Applicant's claims. Most significantly, Achong fails to recognize that apple juice is preferable to a host of other aesthetically pleasing flavors and sweetener ingredients for specific and non-obvious reasons.

To respond: This argument renders moot in view of relying upon Achong Belcheff, Naicker, and Allen in showing that apple juice has many advantages that makes it preferred over other liquids in dissolving or suspending different active agents.

- Applicant has discovered that apple juice has an unexpected advantage and superior results, specifically a superior dissolution profile, when compared to other masking agents

discussed in the prior art, (See also Carrier et al. "Stability and Compatibility of Tegaserod from Crushed Tablets Mixed in Beverages and Food' American Society of Health-System Pharmacists, Inc. (2004), Pages 1138 (3d column), 1140 (3d column), and 1141 (middle column), attached hereto as Exhibit A).

To respond: the dissolution rate is not in the scope of instant claims to be compared to the prior art. Further, dissolution is not an unexpected result of the instant claims since independent claims 1 and 15 recite a suspension not a solution. Finally, as shown hereinabove in the office action, apple juice has many advantages that make the liquid distinguished over other fruit juices. If apple juice has one more advantage then it was decided in court that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case or either anticipation or obviousness has been established, Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nabila G Ebrahim/
Examiner, Art Unit 1618

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618